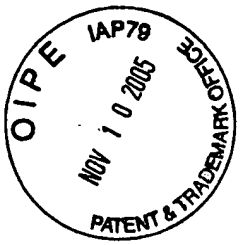
Docket 14249



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

First Named Inventor:	Peter Hagerlid		
Appln. No.:	09/719,960	Group Art Unit:	1634
Filed:	June 14, 2001	Examiner:	B. Sisson
Title:	REACTION MONITORING SYSTEM		

APPELLANT'S BRIEF

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This appeal brief is in response to the final Office Action mailed February 18, 2005 in the above-identified application. This appeal is pursuant to Rule 41.37, following the Notice of Appeal filed July 18, 2005 and received by the Patent Office on July 21, 2005. This paper is accompanied by a petition for an extension of time. A check in payment of the fee set forth in 37 C.F.R. § 41.20(b)(2) and the fee for a two-month extension of time pursuant to 37 C.F.R. § 1.136(b) is enclosed. Any additional fees required by this communication may be charged to Deposit Account No. 50-2054.

I. REAL PARTY IN INTEREST

The real party in interest is Biotage AB, the present name of PyroSequencing AB, owner by assignment of the present patent application.

II. RELATED APPEALS AND INTERFERENCES

Appellants, appellants' legal representative and the assignee are not aware of any prior or pending appeals, interferences or judicial proceedings which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

The present application was originally filed with Claims 1-22. Claims 1-22 were cancelled and Claims 23-45 were added by preliminary amendment. In response to a Restriction Requirement, Claims 23-29 were elected and Claims 40-45 were withdrawn. Claims 40-45 were subsequently cancelled. In response to an Office Action, Claims 25, 26 and 36 were cancelled and Claim 46 was added. The claims on appeal, Claims 23, 24, 27-35, 37-39 and 46, are set

forth in Appendix A. Claims 23, 24, 27-35 and 46 stand rejected under 35 U.S.C. § 103(a). Claims 37-39 have been objected to.

IV. STATUS OF AMENDMENTS

Submitted herewith is an Amendment under Rule 41.33(b)(2) in which Claims 28, 29, 31, 32, 34 and 37 have been amended to independent form.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The presently claimed invention is directed to an apparatus for simultaneously monitoring an array of reaction sites for light. The apparatus comprises a sample receptacle comprising an array of reaction sites and masking means between the reaction sites; a dispenser for dispensing a reagent into samples on the receptacle; a single optically active transducer arranged so that light emitted from samples at the array of reaction sites impinges on corresponding regions of the transducer; a light intensity level determination device; and a recorder that records light intensity level and time of detection thereof for each sample. The apparatus of the invention allows multiple reaction sites to be monitored simultaneously. Multiple reactions can thus be run in parallel, thereby reducing the time for processing of multiple samples. The apparatus is useful for identifying target bases in DNA sequences.

Sample receptacles comprising an array of reaction sites are described, for example, at page 5, lines 1 through 34. The receptacle may comprise a plate, described, for example, at page 5, lines 7-9, which may be in contact with heat regulating means, as described at page 5, lines 25-28.

The masking means between the reaction site in the array of reaction sites is described, for example, at page 5, line 34 through page 6, line 26. As described therein, the masking means may be provided by an opaque coating or channels in a block. The block may comprise a temperature regulating means, as described, for example, at page 6, lines 10-12, and the channels in the block may flare outwardly, as described, for example, at page 6, lines 18-21. The masking means is arranged to reduce the transmission of light between neighboring reaction sites, as disclosed at page 6, lines 2-4.

A dispenser arranged for dispensing a reagent into samples on the receptacle is described, for example, at page 11, lines 29-35.

An optically sensitive transducer is described, for example, at page 4, lines 29-37 and page 6, line 27 through page 8, line 14. The optically sensitive device may be charge coupled device including a frame transfer charge coupled device, disclosed, for example, at page 7, line 29 through page 8, line 10.

A light intensity determination device is disclosed, for example, at page 8, line 5 through page 9, line 27 and page 12, line 28 through page 13, line 9. A converter to convert electrical output to digital signal is described at page 9, lines 1-9. Signals from a plurality of pixels may be converted into a single block, as described at page 9, lines 9-16. A recorder is disclosed, for example, at page 13, lines 9-25, and may record total output from a given site, as described at page 8, lines 22-37.

An apparatus arranged to monitor the reaction sites from underneath is described, for example, at page 5, lines 1-4 and 23-25. An apparatus having an array of lenses between the

reaction sites and the optically sensitive device is disclosed, for example, at page 7, lines 6-28. The lenses in the array may be spaced by a smaller amount than the spaces of the corresponding reaction sites, as described at page 7, lines 19-28.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The single ground of rejection for review upon appeal is the rejection of Claims 23, 24, 27-35 and 46 under 35 U.S.C. § 103(a) as allegedly rendered obvious by U.S. Patent No. 5,874,219 to Rava et al. ("Rava et al.") in view of U.S. Patent No. 5,556,961 to Foote et al. ("Foote et al."). Claims 37-39 have been objected to as allegedly depending upon a rejected base claim.

VII. ARGUMENT

Claims 23, 24, 27-35 and 46 stand rejected under 35 U.S.C. § 103(a) as allegedly rendered obvious by Rava et al. in view of Foote et al. Appellants respectfully submit that a *prima facie* case of obviousness has not been established because: 1) the combination of Rava et al. and Foote et al. does not teach or suggest all of the claim limitations, and 2) there would not have been motivation to combine the references.

A. Prior Art Relied on by Examiner

In the final Office Action mailed February 18, 2005, the Examiner has alleged that Rava et al. teach an apparatus comprising an array of test sites on a chip, and further comprising an array of pixels of a charge coupled device (CCD), which in turn detects signals resulting from a chemical reaction. The Examiner has further alleged that Rava et al. teach that the apparatus can comprise temperature controls, focusing means, and means for collecting and processing data.

The reference also allegedly provides guidance as to how many pixels one would need in a CCD so that a signal at a given test site would be detected and the data recorded. Further, Rava et al. allegedly teach that an array of biological probes may be placed in a well of a microtiter plate to form a "biological chip plate," and that the arrangement of probe arrays in wells can be varied. The Examiner has acknowledged that Rava et al. "do not teach incorporating a mask between the elements or spots of the array." Office Action mailed February 18, 2005 at page 3, line 20.

In the final Office Action it has been further alleged that Foote et al. teach explicitly of incorporating a mask into an array such that the mask has areas of transparency and opacity, wherein the areas of transparency correspond to the reaction sites. The Examiner has alleged that it would have been obvious to incorporate a mask as disclosed by Foote et al with the apparatus of Rava et al. "as the mask of Foote et al. allows for 'a matrix of discrete cells on the surface of a substrate, [with] each cell having precisely defined boundaries so that cells are well defined, individually separated, and at identifiable locations on the substrate.'" Id. at page 4, lines 12-15. The Examiner has alleged that one would have been motivated to incorporate masks into the device of Rava et al. because "Foote et al., at Col. 7, teaches explicitly of their ease and precision of use." Id. at page 4, lines 15-17.

B. Legal Standard

"To reject claims in an application under Section 103, and examiner must show an unrebutted *prima facie* case of obviousness." In re Rouffet, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453, 1455 (Fed. Cir. 1998). The Supreme Court in Graham v. John Deere, 383 U.S. 1, 148 U.S.P.Q. 459 (1966) stated:

> Under Section 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined.

Thus, to establish a *prima facie* case of obviousness, the Examiner has an obligation to construe the scope of the prior art, identify the differences between the claims and the prior art, and determine the level of skill in the pertinent art at the time of the invention. From this, the Examiner must provide a positive reason why it would be obvious to modify the prior art to arrive at the claimed invention. Absent an explanation of "the specific understanding or principle within the knowledge of a skilled artisan that would motivate one with no knowledge of [applicant's] invention to make the combination, [there is an inference] that the examiner selected these references with the assistance of hindsight," which is clearly impermissible. In re Rouffet, 149 F.3d at 1358, 47 U.S.P.Q.2d at 1458 (Fed. Cir. 1998). A positive suggestion or motivation to alter the prior art is a requisite safeguard against hindsight being used to negate patentability. Id. 149 F.3d at 1359, 47 U.S.P.Q.2d at 1459.

When combining references for purposes of demonstrating obviousness of claimed invention, the first requirement is that a suggestion, teaching, or motivation to combine the prior art references be shown. C. R. Bard, Inc. v. M3 Sys. Inc., 157 F.3d 1340, 1352, 48 U.S.P.Q.2d 1225, 1232 (Fed. Cir. 1998). This showing is an "essential evidentiary component of an obviousness holding." Id. This evidence may flow from the (1) prior art references themselves, (2) the knowledge of one of ordinary skill in the art, or, in some cases, (3) from the nature of the problem to be solved. Brown & Williamson Tobacco Corp. v. Philip Morris, 229 F.3d 1120, 1125, 56 U.S.P.Q.2d 1456, 1459 (Fed. Cir. 2000), citing Pro-Mold & Tool Co. v. Great Lakes

Plastics, Inc., 75 F.3d 1568, 1573, 37 U.S.P.Q.2d 1626, 1630 (Fed. Cir. 1996). This showing must be clear and particular, and broad conclusory statements about the teaching of multiple references, standing alone, are not "evidence." Id.

"[M]ultiple cited prior art references must suggest the desirability of being combined, and the references must be viewed without the benefit of hindsight afforded to the disclosure. In re Paulsen, 30 F.3d 1475, 1482, 31 U.S.P.Q.2d 1671, 1676 (Fed. Cir. 1994). It is impermissible to use the inventor's disclosure as a "road map" for selecting and combining prior art disclosures. See Grain Processing Corp. v. American Maize-Products Corp., 840 F.2d 902, 907, 5 U.S.P.Q.2d 1788, 1792 (Fed Cir. 1988). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not be based on Appellant's disclosure. See In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1788 (Fed. Cir. 1991).

To establish obviousness, the prior art references must be evaluated as a whole for what they fairly teach and neither the references' general or specific teachings may be ignored. Application of Lundsford, 357 F.2d 385, 389-90, 148 U.S.P.Q. 721, 724 (CCPA 1966). A reference must be considered for all that it teaches, not just what purportedly points toward the invention but also that which teaches away from the invention. Ashland Oil, Inc. v. Delta Resins & Refractories, 776 F.2d 281, 295, 227 U.S.P.Q. 657, 670 (Fed. Cir. 1985).

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. In re Mills, 916 F.2d 680, 682, 16 U.S.P.Q.2d 1430, 1432 (Fed. Cir. 1990). See also M.P.E.P. § 2143.01. In making the assessment of differences between the prior art and the claimed subject

matter, 35 U.S.C. § 103 specifically requires consideration of the claimed invention "as a whole." This "as a whole" instruction prevents evaluation of the invention part by part. Ruiz v. A.B. Chance Co., 357 F.3d 1270, 1275, 69 U.S.P.Q.2d 1686, 1690 (Fed. Cir. 2004). Without this requirement, an obviousness assessment might break the invention into its component parts, then find a prior art reference corresponding to each component. This improper method would import hindsight into the obviousness determination by using the invention as a roadmap to find its prior art components. Princeton Biochemicals, Inc. v. Beckman Coulter, Inc., 411 F.3d 1332, 1337, 75 U.S.P.Q.2d 1051, 1056 (Fed. Cir. 2005). Simply identifying all of the elements in a claim in the prior art does not render a claim obvious. 35 U.S.C. § 103 requires some suggestion or motivation in the prior art to make the new combination. Id.

C. A *prima facie* case of obviousness has not been established because all of the claim limitations of Claims 23, 24, 27-35 and 46 are not taught or suggested by Rava et al. and Foote et al.

As the Examiner has acknowledged, Rava et al. fail to teach a masking means between the reaction sites of the array on the sample receptacle of the presently claimed apparatus. Appellants respectfully submit that Foote et al. similarly fail to teach or suggest a masking means incorporated between the reaction sites of an array.

In the apparatus of the presently claimed invention, a sample receptacle comprising an array of reaction sites is arranged in connection with a single transducer such that light emitted from a plurality of samples at the array impinges upon corresponding regions of the single transducer. A light intensity level determination device in connection with the single transducer provides simultaneous detection of light from the plurality of samples. The claimed apparatus

thus allows multiple reactions to be run in parallel, and a plurality of light-emitting reactions to be monitored and recorded in real time.

The reaction sites are transparent or partially transparent to allow light emitted therefrom to impinge upon a detection device, either directly or by way of optical means.

A masking means is provided on the sample receptacle and arranged between the reaction sites within the array. The masking means reduces the transmission of light between neighboring reaction sites, i.e., it reduces cross-contamination.

Foote et al. disclose the use of a photolithographic mask in the chemical synthesis of a microarray. Foote et al. do not, as the Examiner has alleged, teach of "incorporating" a mask into an array. Rather, Foote et al. teach a photolithographic method for the synthesis of a microarray. In this method, a photolithographic mask is placed over a derivatized substrate, and light is caused to pass through transparent areas of the mask onto photolabile groups on the substrate. A series of blocking and illumination steps result in production of a microarray having cell areas that are reactive with a selected molecule and boundary areas that are non-reactive. As clearly shown in Figs. 2-4 of Foote et al., the photolithographic mask does not become incorporated into the microarray.

For example, Fig. 2 of Foote et al. depicts a method of synthesizing a microarray. A photolithographic mask (16) is placed over a substrate (10) that has been coated with a photolabile group X. The photolithographic mask has transparent regions (18) and an opaque region (20). Light penetrates the transparent regions and labilizes the X groups that are exposed, leaving a protected portion (22). The photolithographic mask is removed and the substrate is

treated with a non-photolabile blocking group B. A second illumination step (in the absence of a photolithographic mask) results in the formation of a layer (10) having a cell area (26) that is reactive and a boundary area that is non-reactive and non-photolabile. The boundary areas in the array of Foote et al. are thus defined by their chemical non-reactivity, not by a photolithographic mask.

The Advisory Action mailed June 9, 2005 states that "Foote et al., column 12, lines 35-46, teach that there are areas [of the mask] that are opaque as well as transparent, and that the opaque areas can be a virtually any size, shape and arrangement, including that of a border." Appellants respectfully submit that the cited passage does not teach that the opaque areas can be a border. Rather, Foote et al. teach at Col. 12, lines 41-44 that "[t]he opaque portions 534 of the mask 530 may, as shown, be circular and aligned in a close packed hexagonal arrangement to maximize the usable space on the substrate member 524 while maintaining the border areas" (emphasis added). Figure 5, to which the cited passage refers, is a top view of a flow cell for preparing an array. The opaque circular portions of the photolithographic mask at 534 prevent photolabilization of the corresponding regions of the substrate, while the transparent portions of the mask at 536 correspond to areas that will be photolabilized. Clearly, the cited passage and Figure 5 teach a flow cell containing a photolithographic mask having transparent portions surrounding opaque circular areas. Thus it is respectfully submitted that the conclusion in the Advisory Action that "Foote et al. fairly teaches use of a mask that can serve as a border around the reaction sites of an array" is in error. The cited passage and Figure 5 are directed to a flow

cell, not an array, and the border areas around the circular areas in the flow cell correspond to a transparent area of the photolithographic mask.

The Advisory Action mailed June 9, 2005 further states that "Figures 5 and 6 clearly depict an array that comprises a mask." Appellants respectfully disagree. Figures 5 and 6 depict a top view and a cross-sectional view, respectively, of a flow cell for preparing solid-state micro-scale arrays. Foote et al. at Col. 12, l. 3-5. Figures 5 and 6 do not depict an array of reaction sites and masking means between the sites, as claimed herein. Rather, Figures 5 and 6 depict a flow cell in which a photolithographic mask is placed adjacent to a substrate member. The mask as depicted in Figures 5 and 6 has circular opaque areas (534) surrounded by transparent portions (536). The flow cell is used to prepare a microarray that does not contain a photolithographic mask, and in which the boundary areas of the array are provided by non-photolatabile blocking groups linked to the substrates, not by opaque areas of a mask.

The Office Communication mailed August 18, 2005 states that Foote et al. teach, at Col. 3, lines 39-52, of a "second mask, which is retained." Appellants respectfully disagree. The cited passage discloses that, during the synthesis of a microarray, areas are produced that are permanently chemically blocked, i.e., chemically non-reactive. Foote et al. at Col. 3, l. 39-48. This is merely the chemical result of the photolithographic method.

Foote et al. thus fail to teach or suggest a masking means incorporated between the reaction sites of an array. All of the claim limitations are not taught or suggested by Rava et al. and Foote et al., and thus a *prima facie* case of obviousness has not been established.

D. A *prima facie* case of obviousness of Claims 23, 24, 27-45 and 46 has not been established because there would have been no motivation to combine Rava et al. with Foote et al.

The Examiner has alleged that it would have been obvious to incorporate a mask as disclosed by Foote et al. with the apparatus of Rava et al. To the best of Appellants' understanding, the Examiner's position is that the claim elements other than the masking means are met by an embodiment of Rava et al. in which an array of probes (e.g. **640** in Fig. 6) on a chip is attached to the bottom of a well of a microtiter plate. Signals from the array of probes on the chip in the well allegedly impinge upon a detector or chip reader (e.g. **100** in Fig. 1 and **250** in Fig. 2). The Examiner seems to allege that this embodiment could permit "the simultaneous determining of light intensity" of each of the locations of a probe in an array, as stated in the Office Action mailed February 18, 2005 at page 3. The Examiner is thus alleging that it would have been obvious to incorporate a mask between the probes in the array on the biological chip within the microtiter well in the apparatus of Rava et al.

Appellants respectfully submit that even if Foote et al. disclose masking means between the probes in an array (and it does not), one would not have been motivated to include masking means between the probes in the array on the biological chip within the microtiter well in the apparatus of Rava et al. To the contrary, Rava et al. teaches away from the use of masking means in an apparatus that utilizes optical detection.

Rava et al. clearly, repeatedly and consistently teach that the biological chip is transparent to light in embodiments involving optical detection. Specifically, Rava et al. teach that:

> Substrates that are transparent to light are useful when the method of performing an assay on the chip involves optical detection. Col. 4, l. 13-15.
>
> The light passes through the chip plate since it is transparent to at least this wavelength of light. Col. 5, l. 45-46.
>
> In another embodiment, the laser is placed below the biological chip plate and light is directed through the transparent wafer or base that forms the bottom of the biological chip plate. Col. 6, l. 25-28.
>
> FIG. 5 depicts a cross section of this embodiment [of the biological chip plate], showing the wafer 510 having a substrate 520 (preferably transparent to light) and a surface 530 to which is attached an array of probes 540. Col. 8, l. 18-21; Fig. 5.
>
> When the assay is to be performed by sending an excitation beam through the bottom of the plate collecting data through the bottom of the plate, the body of the plate and the substrate of the chip should be transparent to the wavelengths of light being used. Col. 8, l. 63-67.

Accordingly, not only do Rava et al. fail to teach or suggest the use of masking means, but Rava et al. repeatedly teach to the contrary, i.e., that the biological chip is transparent. The reference must be considered as a whole, including the portions cited hereinabove that clearly teach away from the present invention.

Thus there is no suggestion or motivation in Rava et al. to modify its apparatus by incorporating a mask. Foote et al. similarly fail to provide the motivation. Even if, *arguendo*, Foote et al. disclose a mask between the probes of an array (and Appellants submit it does not), Foote et al. do not provide motivation to modify the apparatus of Rava et al. The Examiner alleges only that the "ordinary artisan would have been motivated to have incorporated such masks into the device of Rava et al., for as seen above, Foote et al., at column 7, teaches explicitly of their ease and precision of use." Office Action mailed February 18, 2005 at p. 4. The passage of Foote et al. cited in the Office Action states only that "[p]hotolithographic masks

are easily prepared and positioned with great precision." Foote et al. at Col. 7, l. 14-15. Applicants respectfully submit that such teaching does not provide motivation to combine the references.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. In re Mills, 916 F.2d 680, 682, 16 U.S.P.Q.2d 1430, 1432 (Fed. Cir. 1990). See also M.P.E.P. § 2143.01. Simply identifying all of the elements in a claim in the prior art does not render a claim obvious. 35 U.S.C. § 103 requires some suggestion or motivation in the prior art to make the new combination. Because there is no suggestion or motivation in the prior art to combine the teachings of Foote et al. and Rava et al., a *prima facie* case of obviousness has not been established.

E. A *prima facie* case of obviousness of Claims 28, 29, 31, 32 and 34 has not been established because all of the claim limitations are not taught or suggested by Rava et al. and Foote et al.

The subject matter of Claims 28 and 29 is not rendered obvious by Rava et al. in view of Foote et al. because neither reference teaches nor suggests the element of an array of lenses between the reaction sites and the optically sensitive transducer. The Examiner has alleged that the device of Rava et al. has "focusing means." Rava et al. disclose at Col. 5, lines 63-65 that the "biological chip reader can include auto-focusing feature to maintain the sample in the focal plane of the excitation light." This auto-focusing feature is clearly not an array of lenses as disclosed in Claim 28 nor an array of lenses spaced by a smaller amount than the reaction sites, as claimed in Claim 29.

The subject matter of Claim 31 is not rendered obvious by Rava et al. in view of Foote et al. because neither reference teaches nor suggests the element of a frame-transfer charge-coupled device.

The subject matter of Claim 32 is not rendered obvious by Rava et al. in view of Foote et al. because neither reference teaches nor suggests the element of a means to record a measure of total light output from a given reaction site. Rava et al. disclose at Col. 7, lines 10-19 that a computer that determines fluorescent intensity as a function of substrate position and then calculates binding affinity may be used, and resulting data displayed as an image. However, there is no means to record a measure of total light output in the cited references.

The subject matter of Claim 34 is not rendered obvious by Rava et al. in view of Foote et al. because neither reference teaches nor suggests the element of a means to convert signals from a plurality of pixels into a single block.

Submitted herewith is an Amendment under Rule 41.33(b)(2) in which Claims 28, 29, 31, 32 and 34 have been amended to independent form.

F. Claims 37-39 do not depend upon a rejected base claim.

For all of the reasons discussed in subparts A and B hereinabove and incorporated herein by reference, the subject matter of Claim 23 is not rendered obvious by Rava et al. in view of Foote et al., and thus the objection to Claims 37-39 for depending upon a rejected base claim should be withdrawn. Further, submitted herewith is an amendment under Rule 41.33(b)(2) in which Claim 37 has been amended to independent form.

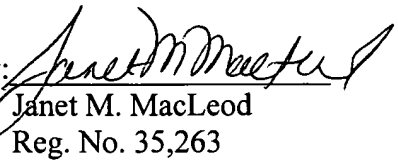
VIII. CONCLUSION

For all of the foregoing reasons, the rejection of Claims 23, 24, 27-35 and 46 under 35 U.S.C. § 103(a) should be reversed.

Respectfully submitted,

DORSEY & WHITNEY LLP

Date: November 2, 2005

By: 

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4821-0501-5040\1

APPENDIX A

CLAIMS ON APPEAL

Claim 23. An apparatus for simultaneously monitoring an array of reaction sites for light indicating that a reaction is taking place at a particular site, comprising:

a sample receptacle for receiving a plurality of liquid samples at said array of reaction sites, said sample receptacle comprising an array of reaction sites and masking means between said reaction sites within said array;

a dispenser arranged for dispensing at least one reagent into said samples on said sample receptacle;

a single optically sensitive transducer arranged so that in use the light emitted from a particular plurality of samples at said array of reaction sites will impinge upon corresponding predetermined regions of said optically sensitive transducer;

a light intensity level determination device in connection with said optically sensitive transducer for simultaneously determining the level of light intensity impinging upon each of said predetermined regions; and

a recorder in connection with said light intensity level determination device for recording said light intensity level and the time of detection thereof for each of said liquid samples.

Claim 24. An apparatus as claimed in Claim 23, wherein said sample receptacle for receiving a plurality of liquid samples comprises a plate.

Claim 27. An apparatus as claimed in Claim 23 arranged to monitor the reaction sites from underneath.

Claim 28. An apparatus as claimed in Claim 23, comprising an array of lenses between, or arranged in use between, said reaction sites and the optically sensitive transducer.

Claim 29. An apparatus as claimed in Claim 28, wherein the lenses of said array are spaced by a smaller amount than the spacing of the corresponding reaction sites.

Claim 30. An apparatus as claimed in Claim 23, wherein the optically sensitive transducer comprises a charge-coupled device.

Claim 31. An apparatus as claimed in Claim 30, wherein the optically sensitive transducer comprises a frame transfer charge-coupled device.

Claim 32. An apparatus as claimed in Claim 23, comprising means to record a measure of the total light output from a given reaction site.

Claim 33. An apparatus as claimed in Claim 23, comprising means to convert the electrical output from said optically sensitive transducer into a digital signal.

Claim 34. An apparatus as claimed in Claim 33, wherein said conversion means converts the signals from a plurality of neighbouring pixels in a single block.

Claim 35. An apparatus as claimed in Claim 24, wherein said plate is in contact with heat regulating means.

Claim 37. An apparatus as claimed in Claim 23, wherein said masking means are provided by channels in a block.

Claim 38. An apparatus as claimed in Claim 37, wherein said block comprises temperature regulating means.

Claim 39. An apparatus as claimed in Claim 37, wherein said channels flare outwardly towards the lower part thereof.

Claim 46. An apparatus for identifying target bases in DNA sequences comprising:

a plate for receiving a plurality of liquid samples at respective reaction sites, said plate comprising a plurality of reaction sites and masking means between said reaction sites;

a dispenser arranged for dispensing at least one reagent into said samples on said plate;

a single optically sensitive transducer arranged so that in use light generated by the reaction of a plurality of particular liquid samples on said plate signifying the incorporation of a nucleotide will impinge upon corresponding predetermined regions of said optically sensitive transducer;

a light level determination device in connection with said optically sensitive transducer for simultaneously determining the level of light intensity impinging upon each of said predetermined regions; and

a recorder in connection with said light intensity level determination device for recording said light intensity level and the time of detection thereof.

APPENDIX B

EVIDENCE APPENDIX

None

APPENDIX C

RELATED PROCEEDINGS INDEX

None